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Melting DNA Yields Clues To the Puzzle of Heredity

UNTIL recently, cross-breeding was the only way biologists could analyze the relationship of two forms with any real precision.

From breeding studies, for example, we know that the amazing range of varieties of dogs all belong to the same species — only a few genes differentiate the hairless Chihuaha from the St. Bernard—while a vast gulf separates the cottontail from the European rabbit. And as far as we know, the main species of higher primates cannot be cross-bred, though it can hardly be said that exhaustive efforts have been made with such combinations as the gorilla and the orangutan and still more exotic combinations might eventually be proven to be cross-fertile.

The double-stranded structure of DNA, the substance within the cells that controls heredity, opens the way to a completely different approach to this problem.

The DNA messages may be compared to the sentences of a book of instructions.

IN THE naturally occurring DNA molecules, the two strands are held together by their mutually complementary structure: the same message is encoded in each strand, but in two complementary languages, so to speak, which we might as well call "plus" and "minus." If solutions of DNA are heated to some 158 degrees Fahrenheit, the double strand structure melts and the strands separate. If the hot solutions are annealed — that is, allowed to cool very slowly — corresponding plus and minus strands may be able to find one another and reform proper double strand molecules.

Obviously, the chance that two corresponding strands can find each other during the annealing will be much larger if most of the molecules are similar to one another than if they fall into many different categories. **In terms of the book analogy, having many copies of the same sentence would make it easier to find matching pairs.**

EARLIER studies on the annealing of DNA were done on simple viruses and bacteria, about which we have a great deal of other information to help corroborate these ideas. By labeling DNA from one species with isotopes, it was possible to study the annealing of DNA from mixed melts with the DNA of another, a method of molecular hybridization that gave an alternative way of studying biological relationships.

The first studies with higher organisms showed that the DNA of a single species can be reannealed with ease that was surprising in view of the expectation that it contained one to ten million different kinds of DNA molecules. On the other hand, even closely related species appeared to be very different by the criterion of molecular hybridization.

Recent reports by biochemists R. J. Britten and D. E. Kohne of the Carnegie Institution of Washington and P. M. B. Walker of the University of Edinburgh have helped to unravel this puzzle and raised striking new ones. A substantial part of the DNA in the cell nuclei of vertebrates — about 30 per cent in the mouse, somewhat less in man — is of a highly repetitious character. That is, the same sequence appears over and over again, a given family of DNA having anywhere from ten to a million duplicate molecules. It is only this "repeated-sequence" DNA that can reanneal rapidly under experimental conditions. The rest of the DNA conforms to previous expectations that it represents just one copy of each of the genes that can be recognized by traditional breeding methods.

The functions of this special DNA are at the moment quite mysterious, as are any reasons for it to differ so markedly among rodent species. (It still remains to be closely studied in primate species and among the races of man.) One speculation that cannot now be contradicted is that the special DNA is a residue of virus infections that have played a hitherto unappreciated role in biological evolution. When human cells are infected with SV-40 virus, at least 20 copies of that DNA can be found in their progeny, in cell cultures. 20

We have long known that salamanders have over ten times as much DNA per nucleus as man. We may now be relieved to hear that most of this is a banal repetitious form and that man is still in the running for being the species with the highest information content in his DNA.